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Nephrology

The impact of Technetium-99m dimercapto-succinic acid scintigraphy on DNA damage and oxidative stress in children

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Abstract

Background: Technetium-99m-dimercapto succinic acid (Tc-99m DMSA) scintigraphy is a commonly used imaging modality in children with urological abnormalities. The radiopharmaceuticals, which have the effects of ionising radiation, are used in this method. This study aimed to investigate the impact of the Tc-99m DMSA scan on renal oxidative stress and mononuclear leukocyte (MNL) DNA damage.

Methods: Children, who were followed up by paediatric nephrology at Bezmialem Vakif University and underwent Tc-99m DMSA scintigraphy between April 2015 and January 2016 with the indication of detection of renal scars, were included in this study. The exclusion criteria were nephrolithiasis, history of premature birth and recent urinary tract infection 3 months prior to scintigraphy or antibiotic use in the last 1 month. 3 mL heparinised blood samples were obtained just before, immediately after and 1 week after the scintigraphy. MNL DNA damage, total antioxidant status (TAS) and total oxidant status (TOS) were measured in the blood samples. The oxidative stress index (OSI) was calculated. Spot urine samples were obtained from each patient before and within 3 days after performing the scintigraphy. TAS/Creatinine (TAS/Cr), TOS/Creatinine (TOS/Cr) and N-acetyl-glucosaminidase/creatinine (NAG/Cr) levels were measured in the urine samples.

Results: Twenty-seven children were evaluated. The values between TAS, TOS and OSI levels in serum samples at baseline, immediately after and 1 week after the scintigraphy ($P = .105$, $P = .913$, and $P = .721$, respectively) showed no statistically significant difference. The levels of TAS/Cr, TOS/Cr, NAG/Cr ratios and OSI, which were evaluated from urine samples before and within 3 days after the scintigraphy scan were also similar ($P = .391$, $P = .543$, $P = .819$ and $P = .179$, respectively). The levels of DNA damage only increased following scintigraphy scan and decreased a week later ($P < .05$).

Conclusions: The effect of Tc-99m DMSA scintigraphy is insufficient to create oxidative damage, but it can cause DNA damage via the direct impact of ionising radiation which can be repaired again in a short time.

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1 | INTRODUCTION

The use of diagnostic radiologic imaging has increased over the last decades, especially computed tomography (CT) and nuclear medicine technology.[1] These procedures deliver high doses of radiation and are epidemiologically linked with radiation-induced cancers.[2] Also, there is an emerging evidence that early life exposure to diagnostic radiation is associated with childhood malignancies.[3,4] Free radicals induced by ionising radiation (such as superoxide, hydrogen peroxide and hydroxyl radicals) react with macromolecules, impair oxidant-antioxidant balance over time and lead to the development of oxidative stress.[5] Oxidative stress is described as the disruption of the balance between free radical production and antioxidant levels in favour of free radicals. This causes molecular damage, which accumulates over time in tissues and cells. DNA damage can lead to mutations, an essential step in carcinogenesis.[6] It is estimated that 2% of future cancers will result from current diagnostic imaging use.[2]

The diagnostic nuclear medicine procedures, that are widely used in the paediatric population, include Technetium-99m-dimercapto succinic acid (Tc-99m DMSA), Technetium-99-m-diethylenetriamine pentaacetic acid (Tc-99m DTPA) and Technetium-99m-mercaptoacetyltriglycine (Tc-99m MAG-3).[7] DMSA plays an essential role in the assessment of renal scarring in febrile urinary tract infections and differential kidney function. Vesicoureteral reflux along with recurrent urinary tract infections are important risk factors for renal damage.[8] The cortical uptake decrease on DMSA is considered as a marker of upper urinary tract infection and an indirect indicator of vesicoureteral reflux and renal scarring.[9] DMSA imaging involves intravenous administration of a radiolabelled tracer that binds to proximal convoluted tubules. The radiation dose delivered by the procedure changes from one institution to another. Michaud et al demonstrated that the mean cumulative radiation dose of DMSA scan per patient approached to those of paediatric chest computed tomography.[10]

Compared with adults, nationwide survey data on radiation-induced risks are limited in the paediatric population. Radiation-related harmful effects of DMSA scan are not well known. Salmanoglu et al showed impaired oxidative and nitrosative balance in adult patients who had undergone DMSA scintigraphy. They showed that malondialdehyde, which is a biomarker of oxidative stress and a lipid peroxidation product, was increased 1.6-fold in the patient group compared with controls.[11] To the best of our knowledge, there is no study conducted with a paediatric population investigating the oxidative stress and DNA damage of DMSA scan. Also, there is no study on possible tubular injury of the radiopharmaceutical used for the scan. N-acetyl-beta-D-glucosaminidase (NAG) is a lysosomal enzyme found in many tissues and, is a widely used urinary biomarker for the diagnosis of renal tubular injury.[12] Urinary NAG is used to detect renal tubular damage in cases such as acute pyelonephritis, vesicoureteral reflux, hydronephrosis, nephrotoxic drug or heavy metal exposure, nephrolithiasis, proteinuria, hyperglycaemia and hypertension.[13]

What's known

Static renal scans using the radioisotope Tc-99m DMSA provide visualisation of focal renal parenchymal abnormalities, assessment of a difference in kidney function and detection of renal scars. This scan has considerable amount of radiation.

What's new

In our study, we showed that Tc-99m DMSA scan did not create oxidative stress, but by analysing mononuclear DNA damage, we demonstrated that it could cause DNA damage via ionising radiation, which could be repaired in a short time.

This study aimed to determine the possible harmful effects and cellular damage of Tc-99m DMSA scintigraphy in the paediatric population by determining radiation-induced renal oxidative stress and mononuclear leukocyte (MNL) DNA damage, and renal tubular injury by urine NAG level measurements.

2 | METHODS

This prospective cohort study involved paediatric patients who were followed up at the outpatient paediatric nephrology clinic of Bezmialem Vakif University and for whom Tc-99m dimercapto- succinic acid (DMSA) scintigraphy was planned between April 2015 and January 2016. The indications included recurrent urinary tract infections and detection of renal scarring with suspicious vesicoureteral reflux. Patients with nephrolithiasis and a history of premature birth, and patients, who had recent urinary tract infection 6 months prior to scintigraphy or who used antibiotics in last 1 month, were excluded from the study. Power calculation was done with the Gpower analysis.[14] In a previous study, Tc-99m pertechnetate thyroid scintigraphy was used and a calculation was performed with the data of mean and standard deviation of dependent variables (92.06 + 13.38 and 79 + 9.43).[15] As a result of the Gpower analysis, the effect size was found to be 0.8. The study sample size determined was 23, if confidence level was 95%, power was 95% and the effect size was 0.8. We included 27 patients with the probability of a percentage of 20% for missing patients.

DMSA scans were performed on a dual-head gamma camera (Symbia E, Siemens Medical Solutions, Hoffman Estates, IL, USA) with a low-energy high-resolution collimator. Images were acquired with anterior-posterior, lateral and oblique projections in 128^2 matrix, 300.000 counts or 5 min per image. In our institution, intravenous hydration, bladder Foley catheter or sedation are not being routinely applied for DMSA scans. Oral hydration was encouraged. Images were acquired 2 to 3 hours after radiotracer injection. Late images were taken as needed. For the paediatric

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TABLE 1 Comparison of serum DNA damage levels and TAS, TOS, and OSI values before, immediately after, and 1 week after injection of the radiopharmaceutical

	1. Group (Before DMSA scintigraphy) Mean ± SD	**2. Group (1 hour after the injection) Mean ± SD**	**3. Group (7 days after DMSA scintigraphy) Mean ± SD**	*P-value*
Serum TAS (n = 18) (μmol Trolox Equivalent/L)	1.202 ± 0.098	1.22 ± 0.07	1.367 ± 0.429	.105*
Serum TOS (n = 15) (μmol H_2O_2 Equivalent/L)	21.63 ± 10.677	21.112 ± 9.771	20.320 ± 5.81	.913**
Serum OSI (n = 15) (AU)	17.433 ± 8.542	17.443 ± 8.333	15.844 ± 3.787	.721**
DNA Damage (n = 24) (AU)	2.125 ± 0.328	4.222 ± 0.41	1.884 ± 0.338	.0001* **P1: .010*** P2: .0001*** P3: .0001*****

Note: Significant *P* values were in bold. Mean ± SD, Mean ± Standard Deviation; n = number of patients.

P1 was the comparison of before DMSA scintigraphy with 1 hour after the injection, *P2* was the comparison of before DMSA scintigraphy and 7 days after DMSA scintigraphy, *P3* was the comparison of 1 hour after the injection and 7 days after DMSA scintigraphy.

*Friedman Analysis of Variance was performed.; **Analysis of Variance was performed.; ***Wilcoxon signed ranks test was used.

population, an activity of 1.85 MBq/kg (0.05 mCi/kg) Tc-99m-DMSA was injected, and the minimum administered activity was 18.5 MBq (0.5 mCi).[16]

2.1 | DNA damage (comet assay)

Three millilitres of heparinised venous blood samples were taken from each patient just before (group 1), immediately after (group 2) and 1 week after the scan (group 3). The groups were composed of the same patients, and they were analysed 3 times. MNL isolation from heparinised blood for the comet assay was performed by density gradient separation (Histopaque 1077; Sigma-Aldrich, Inc, St. Louis, MO, USA). For this purpose, 1 mL of blood was carefully layered over 1 mL of Histopaque and centrifuged for 35 min. at 500 × g and 25℃. The interface band containing MNL was washed with phosphate- buffered saline (PBS) and then collected by 15 min. centrifugation at 400 × g. The resulting pellets were resuspended in PBS to obtain 20.000 cells in 10 mL. MNL DNA damage was evaluated by modifying the alkaline single cell gel electrophoresis (comet assay) method whose principle is based on different migration of DNA molecules with different molecular weights and different electrical charges at alkaline pH. Following electrophoresis, stained DNA can be evaluated by eye or kinetic reading programme when DNA molecules are stained with DNA- specific fluorescent dyes and examined under a fluorescent microscope.[17] In this study, the images of 100 randomly chosen nuclei (50 nuclei from each of two duplicated slides) were analysed visually for each subject. Each image was classified according to the intensity of the fluorescence in the comet tail and was given a value of 0, 1, 2, 3 or 4 (from undamaged, class 0, to maximally damaged, class 4) and the total score of a slide was between 0 and 400 arbitrary units. Samples from each volunteer were displayed on duplicate slides. At least 50 DNAs were imaged on each slide and the total of DNA images was recorded and scored on the computer.

2.2 | Oxidative stress markers and NAG

Blood samples were taken into blood collection tubes and were centrifuged at 3000*g* for 15 min to obtain serum. All serum samples were stored at −80℃ until experiments began. Total antioxidant status (TAS) and total oxidant status (TOS) levels were measured using commercially available kits (Relassay, Turkey) according to Erel's assay. The oxidative stress index (OSI) was defined as the ratio of TOS to TAS and was calculated as follows:

OSI (arbitrary unit) = ([TOS, μmol H2O2 equivalent]/[TAS, μmol Trolox equivalent] × 100).[18,19] Urine samples from each patient were collected just before scintigraphy and within 3 days after scintigraphy. Urinary NAG was analysed using a photometric method (Cobbas 8000 autoanalyzer, Diazyme Laboratories, Poway, CA). TAS, TOS and creatinine levels of the urine samples were also studied and OSI was calculated. The ratio of NAG, TAS and TOS values in spot urine

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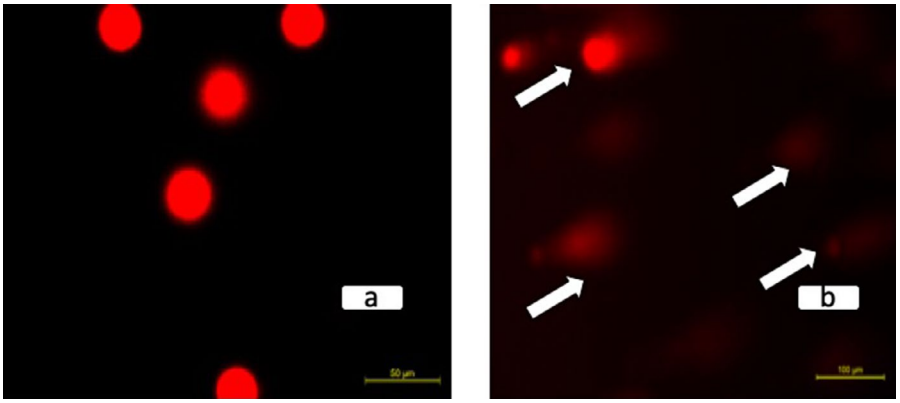

FIGURE 1 (A) Image of normal DNA (B) Image of damaged DNA

to urine creatinine values were used to avoid any effect on dilution and concentration.

2.3 | Statistical analysis

SPSS 20.0 software program was used for statistical analysis of the collected data. Categorical measurements were expressed as number and percentage and numerical computations were expressed as mean and standard deviation. The Shapiro–Wilk test was used for the analysis of compliance with the normal distribution. Continuous variables were summarised by mean±standard deviations, whereas non-parametric variables were shown as median value (Q1 to Q3), where Q is the quartile. The Wilcoxon signed-rank test was used to compare two related samples. Variance analysis was performed to compare the measurements repeated for 3 times with normal distribution, and Friedman analysis was done for parameters with non-normal distribution. In these tests, $P < .0167$ was considered statistically significant as there were three different groups. Wilcoxon signed ranks test was also used for the comparisons of the subgroups. *P* values were expressed as follows: P1 was the comparison of before DMSA scintigraphy with 1 hour after the injection, P2 was the comparison of before DMSA scintigraphy and 7 days after DMSA scintigraphy, P3 was the comparison of 1 hour after the injection and 7 days after DMSA scintigraphy. All statistical tests were two-sided. The results were evaluated at 95% confidence interval, and a *P* value of <0.05 was considered statistically significant excluding the comparison of three subgroups.

3 | RESULTS

Our study included 22 girls and 5 boys aged between 3 months and 15 years. The mean MNL DNA damage levels were analysed in 24 children, and the results of the first group (before scan), second group (immediately after scan), and third group (1 week after the scan) were as follows, respectively: 2.125 arbitrary units (AU), 4.222 AU and 1.885 AU (Table 1). There was a statistically significant difference between the first and second group ($P < .05$) and between the second and third group ($P < .05$; Figures 1, 2). Overall, the mean DNA damage increased just after the scan and decreased 1 week after the scan. Power analysis was done by the Gpower statistical program to detect the power of the study by investigating the groups with statistically significant difference in DNA damage levels (between the first and second group and between the second and third group). The effect size was 5.94 for the difference between the first and second group; 95% confidence level, power was 1. The effect size was 6.54 for the difference between the first and second group; 95% confidence level was 1.

There were no statistically significant difference between the groups in terms of serum TAS, TOS and OSI values ($P > .05$) (Table 1). Because of a storage problem in laboratory, serum TAS levels were evaluated in 18 children and TOS levels were evaluated in 15 children.

TAS/Cr, TOS/Cr, NAG/Cr ratios and OSI levels were evaluated in all children, and the results are illustrated in Table 2. There were no statistically significant differences between the groups (before and after scan) in terms of urine TAS/Cr, TOS/Cr, NAG/Cr ratios and OSI levels (Table 2).

4 | DISCUSSION

To the best of our knowledge, this is the first study investigating the possible harmful effects of Tc-99m DMSA administration in children in terms of oxidative stress, DNA damage and renal tubular injury. We evaluated the levels of ROS in both urine and serum samples, serum MNL DNA damage and a urinary biomarker of acute tubular damage in paediatric patients undergoing Tc-99m DMSA scintigraphy (Tables 1 and 2). Our results showed that MNL DNA damage immediately increased after the scan, but the values decreased to baseline after 1 week (Figure 2). There were no differences between serum and urine oxidative stress levels before and after the DMSA scan and also, urinary NAG levels did not change.

Our study showed that radiopharmaceuticals might exhibit adverse effects on DNA through the direct impact of ionising radiation

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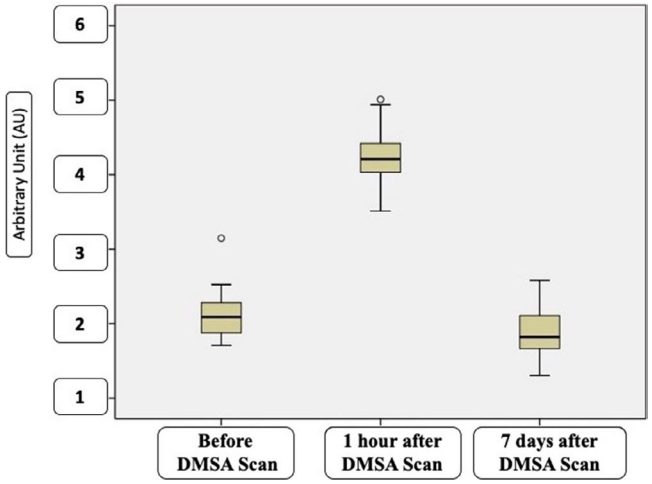

FIGURE 2 Comparison of DNA damage levels. DNA damage occurred just after the DMSA scan and subsequently normalised 1 week later

rather than oxidative damage. The effect of Tc-99m DMSA radiopharmaceutical is not sufficient enough to create oxidative damage. Although DNA damage was repaired, there is no information on the impact of repetitive Tc-99m DMSA or other scintigraphy images on DNA in children. Also, we are not sure if some subtle permanent changes occurred in DNA.

DMSA scans are frequently used in the evaluation of recurrent febrile urinary tract infections in the paediatric population.[7] Paediatric nephrologists and urologists carefully follow up children with renal scars and recurrent urinary tract infections in terms of chronic kidney disease, hypertension and investigate possible underlying vesicoureteral reflux and try to preserve long-term renal function.[10] DMSA scintigraphy involves considerable amount of radiation. The radiation dose in children aged 1-15 years varies between 0.68 and 1.22 mSV (depending on guidelines used). The dose is approximately 1 mSv/examination regardless of the age of the child, adapted according to body surface compared with a paediatric chest CT which is 2-5mSV.[20-22] Cellular exposure to ionising radiation leads to oxidising events, chronic inflammation and has long term effects on genomic instability.[23] It is well known that radiation has carcinogenic effects and paediatric exposure to radiation causes increased lifelong risk for solid cancers and leukaemia.[22]

In recent years, interest in ROS and oxidative stress has increased. ROS has both mutagenic and carcinogenic consequences, affecting many cell components and causing oxidative stress and DNA damage.[6] Studies investigating oxidative stress and ROS after DMSA scan are limited. Salmanoglu showed that oxidative and nitrosative stress was increased in adult patients who were administrated with 99mTc-DMSA compared with the control group.[11] Studies with adult patients who had undergone different scintigraphic techniques demonstrated that antioxidant enzymes decreased after the injection of radiopharmaceuticals.[15,24] In our research, we showed that DMSA administration had no effect on the oxidative stress of children.

DNA is considered to be the primary target for the direct and indirect effects of ionising radiation. The absorption of ionising radiation can cause disruption of atomic structures, radiolysis of water and subsequently damage to nucleic acids, proteins and lipids.[23] The majority of DNA damage is repaired within minutes or hours after induction. However, sometimes, repair cannot be performed or may be incorrect. Both conditions are considered to be a significant risk for carcinogenesis.[25] For these reasons, it is important to investigate possible DNA damage when examining the effects of nuclear imaging techniques using ionising radiation. Some clinical studies have shown that a low dose of iodine-131 might cause chromosomal damages.[26,27] Dantas et al[28] also demonstrated an increased DNA damage in up to 2 hours following Technetium-99m-labelled radiopharmaceutical injection, which is subsequently reduced to zero after 24 hours, consistent with the results of our study. Researchers of the same study interpreted this as the effect of DNA repair mechanisms. In our research, we evaluated DNA damage 1 week later and found that DNA damage was reduced, which initially had increased just after radiopharmaceutical administration.

In recent years, NAG and similar proteins have been commonly discussed in the literature. These proteins can be used as biomarkers for early diagnosis of acute kidney injury.[12,29,30] Several studies in the literature demonstrated that urinary NAG excretion is a very sensitive parameter in determining renal tubular damage, and levels can change when exposed to hypoxic, toxic, and even radioactive substances.[12,29-31] It has been affirmed that increased ROS levels are associated with high urinary NAG excretion and renal tubular damage.[32] In our study, we analysed the possibility of renal tubular influence in addition to oxidative damage in the early period by evaluating urinary NAG excretion. Urinary NAG, TAS, TOS and OSI levels did not change after the administration of DMSA radiopharmaceutical. The absence of oxidative damage in the urine samples is a consistent finding along with lack of increase in urinary NAG levels. It also supports the absence of oxidative damage in serum examination. According to these results, there was no short- or long-term renal tubular damage after the first DMSA scintigraphy. This might be because of the short-acting and low-dose radiation received from Tc-99m DMSA.

There are some limitations in our study. First, the study sample size was small and had a wide age range distribution. Another limitation was the fact that we were not able to analyzs the serum levels of TAS, TOS and OSI for all children owing to technical reasons. Also, we did not include a control group without previous urinary tract infection because of ethical concerns. Our study group did not have a history of infection in the last 6 months. However, previous infections might have influenced renal tubular function. The results may be misleading especially in individuals in whom DMSA shows renal scarring, which reflects kidney fibrosis and/or altered cellular structure/metabolism. Other limitations were as follows: we did not directly quantify the radiation dose delivered by the DMSA scan and we did not study other potential imaging studies that might have caused similar oxidative stress injury or DNA damage such as CT scans. Lastly, we did not determine the exact time of the recovery of DNA damage and did not study the effect of repetitive DMSA scans. The strengths of our study included

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TABLE 2 Comparison of TAS/Cr, TOS/Cr, OSI, and NAG/Cr values in urine obtained before DMSA scintigraphy performed and within 3 days after scintigraphy

	1. Group (Before DMSA scintigraphy) Mean ± SD	2. Group (Within 3 days after scintigraphy) Mean ± SD	*P-value*
Urine TAS/Cr (n = 27) (μmol Trolox Equivalent/g)	0.0749 ± 0.042	0.066 ± 0.033	.391*
Urine TOS/Cr (n = 27) (μmol H_2O_2 Trolox Equivalent/g)	0.273 ± 0.2	0.219 ± 0.342	.732*
Urine OSI (n = 27) (AU)	2.75 ± 2.2	3.45 ± 1.91	.179*
Urine NAG/Cr (n = 27) (U/g creatinine)	0.144 ± 0.113	0.105 ± 0.114	.819*

Note: Urine TAS/Cr: Urine NAG/Cr ratios; Urine TOS/Cr: Urine TOS/Cr ratios; Urine NAG/Cr: Urine NAG/Creatinine ratios. Mean ± SD, Mean ± Standard Deviation; n, number of patients.

*Wilcoxon Signed Ranks test was performed.

evaluation of oxidative stress, DNA damage and renal tubular damage markers before and after the DMSA scan in the paediatric population. Many families have concerns about the adverse effects of DMSA scan in terms of ionising radiation and renal damage. In clinical practice, our data showed that DMSA scan did not cause oxidative stress and tubulopathy and the DNA damage was not permanent.

In conclusion, the MNL DNA damage increased just after the administration of Tc-99m DMSA radiopharmaceutical in children and normalised after 1 week. This finding suggests that DNA damage caused by radiopharmaceuticals is reversible. However, this does not exclude smaller permanent changes, which may be demonstrated by other techniques. DMSA scan was not associated with an increased oxidative stress or renal tubular damage in this study. Further researches with larger sample sizes are warranted in the future.

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Not applicable.

DISCLOSURE

The authors have no conflict of interest to declare.

AUTHORS' CONTRIBUTIONS

SV, FÖ and ADD conceived the present idea. SV carried out the experiments and sample collection and prepared the first draft of the manuscript. AK and EK performed the laboratory assay, and analysis AK performed the statistical analyses. MA performed nuclear medicine procedures. SV, FÖ, ADD and NG participated in the study design, interpretation of data, drafting of the manuscript and approved the final version of the manuscript. NG and TI contributed to the interpretation and critically revised the text. All authors have read and approved the manuscript.

ETHICS DECLARATIONS

Informed consents were obtained from all parents. This study was approved by the Clinical Research Ethics Committee of Bezmialem Vakif University (no.71306642-050.01.04-6/10).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available because of privacy or ethical restrictions.

REFERENCES

1. Mettler FA Jr, Bhargavan M, Faulkner K, et al. Radiologic and nuclear medicine studies in the United States and worldwide: frequency, radiation dose and comparison with other radiation sources—1950-2007. *Radiology*. 2009;253(2):520-531.
2. Smith-Bindman R, Miglioretti DL, Johnson E, et al. Use of diagnostic imaging studies and associated radiation exposure for patients enrolled in large integrated health care systems, 1996–2010. *JAMA*. 2012;307(22):2400-2409.
3. Linet MS, Kim KP, Rajaraman P. Children's exposure to diagnostic medical radiation and cancer risk: epidemiologic and dosimetric considerations. *Rediatr Radiol*. 2009;39(Suppl 1):S4-S26.
4. Brenner DJ, Hall EJ. Computed tomography – an increasing source of radiation exposure. *N Engl J Med*. 2007;357(22):2277-2284.
5. Koç U, Tan S, Ertem AG, Gumus M, Ozbek B, Erel O. Evaluation of thiol-disulphide homeostasis in radiation workers. *Int J Radiat Biol*. 2017;93(7):705-710.
6. Valko M, Rhodes CJ, Moncol J, Izakovic M, Mazur M. Free radicals, metals and antioxidants in oxidative stress-induced cancer. *Chembiol Interact*. 2006;160(1):1-40.
7. Dhull RS, Joshi A, Saha A. Nuclear imaging in pediatric kidney diseases. *Indian Pediatr*. 2018;55(7):591-597.
8. Nordenström J, Sjöström S, Sillen U, Sixt R, Branström P. The Swedish infant high-grade reflux trial: UTI and renal damage. *J Pediatr Urol*. 2017;13(2):146-154.
9. Kim D, Yoon HJ, Woo SH, et al. Development of visual scoring system with Tc-99m DMSA renal scintigraphy to predict the risk of recurrence of symptomatic urinary tract infections in pediatric patients. *Ann Nucl Med*. 2019;33(9):708-715.
10. Michaud JE, Gupta N, Baumgartner TS, Kim B, Bosemani T, Wang MH. Cost and radiation exposure in the workup of febrile pediatric urinary tract infections. *J Surg Res*. 2016;203(2):313-318.
11. Salmanoglu E, Kurutas EB. The levels of oxidative and nitrosative stress in patients who had 99mTc-MIBI myocardial perfusion scintigraphy and 99m Tc-DMSA, 99mTc-MAG-3 renal scintigraphy. *Nucl Med Rev Cent East Eur*. 2020;23(2):89-96.
12. Ding W, Mak RH. Early markers of obesity-related renal injury in childhood. *Pediatr Nephrol*. 2015;30:1-4.

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13. Waring WS, Moonie A. Earlier recognition of nephrotoxicity using novel biomarkers of acute kidney injury. *Clin Toxicol (Phila)*. 2011;49(8):720-728.
14. Faul F, Erdfelder E, Buchnet A, Lang AG. Statistical power analysis using G*power 3.1: tests for correlation and regression analysis. *Behav Res Methods*. 2009.
15. Çiçek E, Yıldız M, Delibaş N, Bahçeli S. The effects of thyroid scintigraphy studies on oxidative damage in patients. *Acta Physiol Hung*. 2006;93(2–3):131-136.
16. Piepsz A, Colarinha P, Gordon I, et al. Guidelines for 99mTc-DMSA scintigraphy in children. *Eur J Nucl Med*. 2001;28(3):BP37-BP41. (Revised in 2009).
17. Singh NP, McCoy MT, Tice RR, Schneider EL. A simple technique for quantitation of low levels of DNA damage in individual cells. *Exp Cell Res*. 1988;175(1):184-191.
18. Erel O. A new automated colorimetric method for measuring total oxidant status. *Clin Biochem*. 2005;38(12):1103-1111.
19. Erel O. A novel automated method to measure total antioxidant response against potent free radical reactions. *Clin Biochem*. 2004;37(2):112-119.
20. Smith T, Evans K, Lythgoe MF, et al. Radiation dosimetry of Tc-99m DMSA in children. *J Nucl Med*. 1996;37:1336-1342.
21. Jang SJ. Nuclear medicine in pediatric urology. *Child Kidney Dis*. 2015;19:14-22.
22. Miglioretti D, Johnson E, Williams A, et al. The use of computed tomography in pediatrics and the associated radiation exposure and estimated cancer risk. *JAMA Pediatr*. 2013;167(8):700-707.
23. Azzam EL, Jay-Gerin JP, Pain D. Ionizing radiation-induced metabolic oxidative stress and prolonged cell injury. *Cancer Lett*. 2012;327(1-2):48-60.
24. Çiçek E, Yıldız M, Delibaş N, Bahçeli S. The effects of 201Tl myocardial perfusion scintigraphy studies on oxidative damage in patients. *West Indian Med J*. 2009;58(1):50-53.
25. Dobrzyńska MM, Pachocki KA, Gajowik A, Radzikowska J, Sackiewicz A. The effect occupational exposure to ionizing radiation on the DNA damage in peripheral blood leukocytes of nuclear medicine personnel. *J O Health*. 2014;56(5):379-386.
26. Rodrigues CL, Corb R, Martins FPP, Barbosa da Fonseca LM, Aranha IP, Gutfilen B. Low dosage of 131iodine effects on chromosomes. *Yale J Biol Med*. 2003;76(3):109-114.
27. Erselcan T, Sungu S, Ozdemir S, Turgut B, Dogan D, Ozdemir O. Iodine-131 treatment and chromosomal damage: in vivo dose-effect relationship. *Eur J Nucl Med Mol I*. 2004;31(5):676-684.
28. Dantas FJ, De Mattos JC, Moraes MO, et al. DNA damage in peripheral blood nuclear cells assessed by comet assay from individuals submitted to scintigraphic examinations. *Cell Mol Biol*. 2002;48(7):789-791.
29. Haase M, Bellomo R, Devarajan P, Schlattmann P, Haase-Fielitz A, NGAL Meta-analysis Investigator Group. Accuracy of neutrophil gelatinase-associated lipocalcin (NGAL) in diagnosis and prognosis in acute kidney injury; a systematic review and meta-analysis. *Am J Kidney Dis*. 2009;54(6):1012-1024.
30. Göknar N, Öktem F, Arı E, Demir AD, Torun E. Is oxidative stress related to childhood urolithiasis? *Pediatr Nephrol*. 2014;29(8):1381-1386.
31. Nguyen MT, Devarajan P. Biomarkers for the early detection of acute kidney injury. *Pediatr Nephrol*. 2008;23(12):2151-2157.
32. Nath KA, Norby SM. Reactive oxygen species and acute renal failure. *Am J Med*. 2000;109(8):665-678.

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